Are Early Feasibility Studies an orphan approach in the regulatory pipeline for medical devices clinical maturity?

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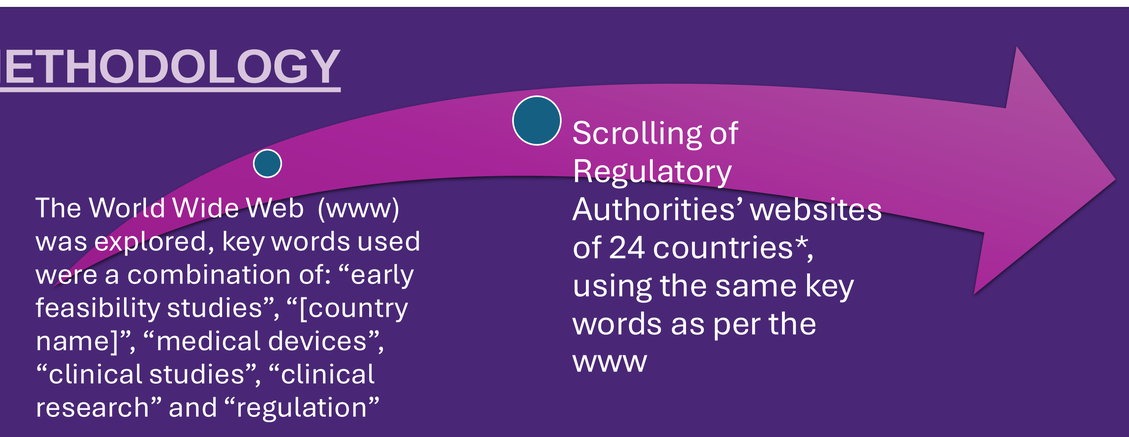
RESEARCH MOTIVATION

While USA has an Early Feasibility Studies (EFS) regulation since 2011 that gives clear guidance on developing EFS of new breakthrough medical devices (MD), in the European Union (EU) there is not such regulation. The lack of clear rules on EFS discourages clinical research and investments in innovation development in the EU. The HEU-EFS, an EU granted Innovative Health Initiative project, aims to formulate recommendations for the establishment of an EFS Program within the EU, with a focus on ensuring patient safety and enhancing the EU single market competitiveness. To start with any approach to solve the mentioned regulatory gap, an exploratory analysis of how different countries are regulating the execution of EFS for medical devices is needed.

OBJECTIVE

To describe the state of the art and similarities and differences of current regulatory policies on EFS regulations (or EFS-like) at national level in the G-20 and BRICS countries for MD to identify key elements for a future EU EFS regulation.

METHODOLOGY



*Argentina, Australia, Brazil, Canada, China, USA, Ethiopia, France, Germany, India, Indonesia, Iran, Italy, Japan, Mexico, Rusia, Saudi Arabia, South Africa, South Korea, Spain, Turkey, Egypt, United Arab Emirates, United Kingdom

RESULTS

2 out of 24 countries have been identified to have an explicit EFS or EFS-like regulation: USA and Australia

For a EFS regulation, the key thematic sections to be included are: type of medical devices targeted, application process, pre-clinical evidence needed, patient protection measures, selection criteria for centers, selection criteria for patients and design iterations and controls (1).
USA regulation was the most comprehensive with 7 key thematic sections included. The Australian regulation considers just 3 of them. Table 1 shows the comparative results between regulations. Similarities between countries are written in green, differences in black and missing information in orange.

Table 1. Comparison of the key thematic sections of EFS-like regulatory policies.

COUNTRY	COMPETENT AUTHORITY CONCERNED	TYPE OF MEDICAL DEVICES	APPLICATION PROCESS	PRE-CLINICAL EVIDENCE NEEDED	PATIENT PROTECTION MEASURES	SELECTION CRITERIA FOR CENTERS	SELECTION CRITERIA FOR PATIENTS	DESIGN ITERATIONS AND CONTROLS
USA	**FDA**	Device early in development, typically before the device design has been finalized, for a specific indication (e.g., innovative device for a new or established intended use, marketed device for a novel clinical application).	Developers should: 1. Contact an EFS Program representative. 2. Submit a Pre-Submission. 3. Engage with CDRH to request feedback. 4. Submit an IDE application.	1. Device Attributes 2. Potential Failure Modes 3. Potential Device and Clinical Effects of Failure 4. Design Information 5. Nonclinical and Supportive Clinical Information, 6. Non-clinical Testing 7. Mitigation Strategies	An informed consent form complying with the requirements in 21 CFR 50.25 and should address the distinctive aspects of an early feasibility study.	Standard and additional risk mitigation strategies include the use of study sites that have sufficient expertise and resources to manage adverse events and provide appropriate alternative therapies if needed	Ensure adequate capture of adverse clinical events and device performance information. Justification regarding the amount and type of information/data needed to support initiation of the study in the specified patient population.	1. Changes requiring FDA **notification** (5-day notice). 2. Changes requiring FDA **approval**: • Contingent approval: prior FDA approval. • Interactive review: informal discussions with FDA during 30-day review cycle.
AUSTRALIA	**TGA**	Device introducing new technology, material or treatment concept. Also considered for medical devices that pose a risk of serious patient harm.	1. Sponsor application to the TGA. 2. TGA evaluation. 3. HREC evaluation. 4. Sponsor notification of each trial conducted.	Engineering analysis and testing, computational simulation, biocompatibility and animal testing.	No difference from pre-market pivotal or post-market stage, except the indicative sample size: • Pre-market pilot: 10-30 • Pre-market pivotal: 100 • Post-market: 1000	EFS studies do not receive special consideration.	EFS studies do not receive special consideration.	EFS studies do not receive special consideration.

TGA: Therapeutic Goods Administration; **FDA**: Food & Drug Administration; **HREC**: Human Research Ethics Committees; **CDRH**: Center for Devices and Radiological Health

CONCLUSIONS: EFS are still an orphan regulatory approach for MD since only 2 countries among the 24 explored have been identified to have EFS or EFS-like regulations. These available regulations could inspire an EU EFS policy aimed to equilibrate innovation with safe MD development and attract clinical research and investments in innovation development in the EU.

REFERENCES: (1) Callea G, Federici C, Freddi R, Tarricone R. Recommendations for the Design and Implementation of an Early Feasibility Studies Program for Medical Devices in the European Union. Expert Rev Med Devices. 2022;19(4):315-325. doi:10.1080/17434440.2022.2075729.

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